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EVIDENCE BRIEF

(ARCHIVED) SARS-CoV-2 Omicron Variant Sub-Lineage BA.2.75

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Key Messages

- There are insufficient data on the transmissibility, severity, and immune evasion of the Omicron sub-lineage BA.2.75 (referred to informally by some as "Centaurus") to assess its risk to Ontarians.
- There are nine spike (S) gene mutations reported for BA.2.75 in addition to its BA.2 S gene mutations, and several had not been previously identified in a variant of concern (VOC) or variant of interest (VOI).
- BA.2.75 has 11 mutations that are distinct from BA.5 (the current predominant lineage in Ontario).
- The earliest documented sequences of BA.2.75 were from India in May 2022, and sequences that may be BA.2.75 have been identified in at least 10 other countries at this time, including Canada.

Issue and Research Question

There are multiple PANGO sub-lineages associated with the B.1.1.529 (Omicron) VOC. The main BA.1, BA.2, BA.3, BA.4, and BA.5 sub-lineages also have their own sub-lineages (e.g., BA.1.1, BA.2.12, BA.2.12.1, BA.2.3, BA. 2.20, BA.2.9, BA.5.1, BA.5.3.1). Considering the possible changes to transmissibility, severity, and/or vaccine effectiveness (VE) of these sub-lineages compared to other VOCs, it is important to monitor the potential impact they might have in Ontario's context.

The World Health Organization (WHO) has designated the Omicron sub-lineage BA.2.75 as a VOC lineage under monitoring (LUM),[1,2] and the European Centre for Disease Prevention and Control (ECDC) has designated it a variant under monitoring (VUM).[3] BA.2.75 is unofficially referred to in media as "Centaurus".

This evidence brief summarizes available information and evidence on the Omicron variant sub-lineage BA.2.75 relevant to the risk of transmission in Ontario.

Methods

Public Health Ontario (PHO) Library Services has been conducting daily searches of primary and preprint literature on Omicron variants and sub-lineages using the MEDLINE database (search strategies available upon request).[4] Preprints are research papers that have not undergone peer-review but are made publicly available to provide the latest data relevant to the rapidly evolving COVID-19 pandemic. PHO performed grey literature searches daily using various news feeds and custom search engines. English-language peer-reviewed and preprint records that described the Omicron sub-lineage BA.2.75 were included if identified.

Genomic Features

- BA.2.75 does not carry the S gene deletion at amino acid positions 69-70 (del69-70) and therefore does not exhibit the S-gene target failure (SGTF) pattern on some molecular assays.

- In addition to S gene mutations seen in BA.2, BA.2.75 contains the following nine S gene mutations: K147E, W152R, F157L, I210V, G257S, D339H, G446S, N460K, and Q493 (reversion).[2] As a comparison, BA.4 and BA.5 have four S gene mutations in addition to BA.2 mutations (del69-70, L452R, F486V, and Q493 [reversion]), and exhibit considerable evasion of neutralizing antibodies from prior SARS-CoV-2 infections and current vaccines.[5] [6,7]

- The impact of the BA.2.75 S gene mutations in combination is unclear at this time.

    - G446S is one of the most potent sites of escape from antibodies elicited by current vaccines and is infrequently found in BA.1.19 and BA.1.15.2.[8,9]

    - Q493 is the original amino acid found in the wild-type SARS-CoV-2 lineages. This is considered a reversion from the BA.2 mutation Q493R, BA.2.75's parent lineage. Other Omicron lineages harboring the wild-type Q493 include BA.4 and BA.5. The original Q493 amino acid is thought to have higher receptor affinity and improves SARS-CoV-2 fitness as compared to the Q493R mutation.[7]

    - K147E, W152R, F157L, I210V, G257S, G339H, and N460K have not been identified in a previous VOC or VOI but have been individually reported in rare lineages. [10]

- The unique BA.2.75 S gene mutations are located in the N-terminal and receptor-binding domains of the S protein, which tend to be more prone to mutations due to being targeting sites of neutralizing antibodies.[11]

- Except for Q493 (reversion), all other mutations that distinguish BA.2.75 from BA.2 also distinguish BA.2.75 from BA.4 and BA.5. In total, there are 11 distinct mutations between BA.2.75 and BA.5, and 12 distinct mutations between BA.2.75 and BA.4. The large number of distinct mutations is of concern as they may result in BA.2.75 evading immunity generated by BA.5 infections, similarly to how BA.5 has increased immune escape following BA.2 infections.

- BA.2.75 has five additional mutations beyond the S gene: non-structural protein 3 (NSP3):S403L (also known as ORF1a:S1221L), NSP3:P822S (also known as ORF1a:1640S), non-structural protein 8 (NSP8):N118S (also known as ORF1a:N4060S), open reading frame 1b (ORF1b):G662S, and envelope (E): T11A.

- There are no mutations involving the main protease (M^{pro}) protein, the current target site of nirmatrelvir/ritonavir (Paxlovid).

Epidemiology

- The earliest documented sequences of BA.2.75 were reported from India in May 2022, and were identified in geographically opposite regions of the country.[2] Over 30% of the increase in daily reported COVID-19 cases in India are believed to be BA.2.75.[12]

- BA.2.75 has now been detected in at least 10 other countries, including Australia, New Zealand, Germany, Luxembourg, Nepal, the United Kingdom, the United States, and Canada.[13-15]

    - As of July 6, 2022, the Public Health Agency of Canada (PHAC) estimated 5 detections of BA.2.75 in Canada, based on the preliminary definition at that time.[16]

Ontario Risk Assessment

There are insufficient data on the transmissibility, severity and immune evasion of the Omicron sub-lineage BA.2.75 to assess its risk to Ontario.[3]

Implications for Public Health Practice

The high number of unique mutations in the BA.2.75 sub-lineage merits close monitoring of local whole genome sequencing (WGS) surveillance and local epidemiology. Epidemiological indicators from jurisdictions reporting BA.2.75 sequences can also be informative, but the epidemic curve experienced in India, for example, may not be generalizable to the Ontario context due to differences in history of previous SARS-CoV-2 infection, vaccination status, public health measures, as well as age distribution of the population.

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